UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,197	10/18/2005	Holly Prentice	2159.0580001/EKS/LMB	8404

53644 7590 04/02/2008

STERNE, KESSLER, GOLDSTEIN & FOX, P.L.L.C.
1100 NEW YORK AVE., N.W.
WASHINGTON, DC 20005

EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
04/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,197	PRENTICE, HOLLY	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *63* is/are allowed.

6)☒ Claim(s) *22-62 and 64-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/14/06,9/12/06,11/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, nucleotide and amino acid sequences present in the specification and drawings have not been identified by the appropriate SEQ ID NO identifiers.

The nature of the Sequence Rule non-compliance does not however, preclude an examination of the application on the merits, the results of which are communicated below.

35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 22-30, 33, 36-38, 41-43, 50-54,56 and 65-70 are rejected under 35 U.S.C. 102(e) as being anticipated by Perkins et al.

Applicant claims a genetic vector for stable transfection and expression of a desired protein within eukaryotic cells comprising: (a) distal 5' flanking sequences of a eukaryotic locus; (b) proximal 5' regulatory sequences of a eukaryotic locus; (c) at least a first insertion site for a first heterologous coding sequence; and (d) proximal 3' regulatory sequences effective for transcription termination of a eukaryotic locus; wherein said sequences are operably joined in order (a)-(d) in a 5' to 3' orientation, with optional linker sequences between adjacent sequences; and wherein (1) said distal 5' flanking sequences comprise a sequence of at least 100 bases having at least 70% identity to a nucleotide sequence found between 20 bp and 100,000 bp 5' of a transcriptional initiation site of a ferritin heavy chain locus; or (2) said proximal 5' regulatory sequences comprise a sequence of at least 20 bases having at least 70% identity to a nucleotide sequence found between 1 bp and 10,000 bp 5' of a translational initiation codon of a ferritin heavy chain locus.

Perkins et al. (US 20030119104, published 6/26/03, filed 5/20/2002, see whole document, particularly the Abstract, paragraphs [0098], [0210], [0241], [0245], [0316]-[0318]) teaches genetic vectors for stable transfection and expression of a desired protein within eukaryotic cells, said vectors comprising sequences from the human ferritin heavy chain promoter (see SEQ ID NO:128) wherein said sequence comprises ferritin promoter sequences which are encompassed within the distal and proximal 5' regulatory regions (as defined by applicants). The vectors disclosed by Perkins et al.

can comprise at least one insertion site (i.e. a multiple cloning site) for a heterologous sequence. The human ferritin heavy chain promoters disclosed by Perkins et al. include untranslated exon sequences (i.e. beginning at position 269 of SEQ ID NO:128, see also Hentze et al. PNAS, 1986, Vol. 83, pp. 7226-7230, Fig. 2, cited by applicants, for the human ferritin heavy chain promoter nucleotide sequence). With regard to the proximal and distal 3' regulatory sequences (i.e. polyA sequences), the vectors of Perkins et al. comprise polyA sequences which can be from SV40 or any other suitable source and can comprise a sequence such as AATAAA (i.e. containing a sequence at least 70% identical to a nucleotide sequence found within the 3' regulatory region of a ferritin heavy chain locus). Perkins et al. also teaches eukaryotic cells comprising said vectors and use of said cells for expression of proteins of interest. Perkins et al. therefore teaches the claimed invention.

35 USC 103(a) Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 34, 39-40 and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perkins et al. in view of Kwak et al.

Applicant's invention is as recited in the above 35 USC 102(e) rejection. Additionally, applicant claims that the 5' flanking regions in the vector can comprise

ferritin heavy chain locus 5' sequences with a total length of between 1,000 and 10,000 bases or at least 500 nucleotides found between 1 bp or between 20 bp up to 10,000 bp from the translation initiation codon of a ferritin heavy chain locus or at least 70% identity to said sequences.

Perkins et al. is applied as above. Perkins et al. does not teach ferritin 5' regulatory regions of the size claimed by applicant.

Kwak et al. (cited by applicants, J. Biol. Chem., 1995, Vol. 270, No. 25, pp. 15285-15293, see whole article, particularly the Abstract, p. 15291-15292) teaches important regulatory elements in the ferritin heavy chain gene promoter located several kb (~4.8 kb) to the transcriptional start site as well as NF-κB consensus motifs within the first 941 nucleotides in the 5' flanking region, etc.

The claimed invention involves size ranges of ferritin heavy chain gene promoter sequence or sequences at least 70% identical to said sequences. The extensive promoter region of the ferritin heavy chain gene was well known in the prior art and contained elements located up to at least several kb upstream of the transcriptional start site (see for example Kwak et al.).

The ordinary skilled artisan, seeking to use a ferritin heavy chain gene promoter sequence for expression of genes of interest in a vector would have been motivated to use some or all of the sequences in the promoter which direct or enhance expression so as to increase the versatility of the promoter for expression of genes of interest operably linked to said promoter. The prior art, as exemplified by Kwak et al. teaches that the ferritin heavy chain gene promoter region comprises multiple elements over several kb

of sequence which direct activity of the promoter and the ordinary skilled artisan would have been motivated to include those sequences, which can be up to several kb in length, in the vector so as to provide a promoter with the versatility of the naturally occurring ferritin heavy chain gene promoter. It would have been obvious for the ordinary skilled artisan to include sequences at least 500 bases or between 1,000 to several thousand bases from the ferritin heavy chain gene promoter because Perkins et al. teaches that a ferritin heavy chain gene promoter can be used in recombinant expression vectors and because Kwak et al. teaches important additional promoter elements located in regions up to several kb 5' from the transcriptional start site of the ferritin heavy chain gene. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 35, 55 and 57-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perkins et al. in view of Kaufman (US 4,740,461).

Applicant's invention is as described above. Additionally, applicant claims that the vector comprises 3' regulatory sequences having a total length of 1000-10000 bases or 3' regulatory sequences of at least 100 or 500 or 1000 bases and at least 70% or 80% or 90% or 100% identical to the nucleotide sequence found within the distal 3' flanking region of a ferritin heavy chain locus.

Perkins et al. is applied as above. Perkins et al. does not teach the 3' regulatory regions of the recited length or 3' regulatory regions for the ferritin heavy chain gene locus and inclusion of these sequences in a vector.

Kaufman (see whole document, particularly columns 7-8) teaches that expression vectors normally comprise polyadenylation sequences which can be positioned downstream of the gene of interest and can be from any source and the 3' region can comprise a untranslated nucleotide sequence of up to about 1,000 bases from the stop codon to the polyadenylation site followed by an additional 200-600 bp of sequence downstream of the polyadenylation site.

The ordinary skilled artisan, seeking to design an expression vector, would have been motivated to include a polyadenylation sequence because Perkins et al. teaches that a polyadenylation sequence is included in the vectors disclosed by Perkins et al. and said skilled artisan would have been motivated to include a polyadenylation signal sequence of the size claimed and from the ferritin heavy chain gene sequence because Perkins et al. teaches that a polyadenylation signal is included in expression vectors comprising a ferritin heavy chain promoter sequence and Kaufman teaches that polyadenylation sequences and 3' flanking sequences can be up to 1,000 bases or more and can be from any source and that the inclusion of untranslated sequence (up to 1,000 bases) downstream of the stop codon and upstream of the polyadenylation site tends to enhance product yields. It would have been obvious to use the ferritin heavy chain gene 3' flanking region since this is from the same source as the promoter and because Kaufman and Perkins et al. teach that any polyadenylation region can be used

in expression vectors. Additionally, the 3' flanking region is being used for its known and expected function, i.e. to terminate gene expression in the vector. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perkins et al. in view of either Eglitis et al. or Hillgenberg et al.

Applicant's invention is as described above. Additionally, applicant claims a genetic vector with an insertion site of 0, 1, 2, 3, 4 or 1000 or 5,000 bp.

Perkins et al. is as described above. Perkins et al. teaches multiple cloning sites in the vector but does not explicitly recite the length of the insertion sites.

Eglitis et al. (US 5,672510, see whole document, particularly column 6) and Hillgenberg et al. (US 20020001579, published 1/3/2002, see whole document, particularly paragraph [0026]) teach insertion sites for foreign nucleic acid sequences in the context of vectors. The insertion sites can be multiple cloning sequences or any piece of nucleic acid with suitable restriction cleavage sites.

Applicant claims vectors with insertion sites of various sizes. Perkins et al. teaches the claimed vectors with multiple cloning sites which contain multiple restriction endonuclease cleavage sites. Each cleavage site can be considered an insertion site and a given multiple cleavage site can contain sites for blunt end restriction enzymes or sequences of 1 or 2 or 3 or 4 bases which can be sites of endonuclease cleavage or the

insertion site can be any length of DNA with suitable restriction endonuclease cleavage sites, as noted by Hillgenberg et al.). Essentially all expression vectors have sites for insertion of foreign nucleic acid sequences as the vectors are designed to accommodate foreign sequences for expression in host cells. It would have been obvious for the ordinary skilled artisan to include insertion sites of the claimed type in the vectors described by Perkins et al. because insertion sites for insertion of heterologous sequences of interest into vectors are standard in the construction of expression vectors and any sequence (of any size) can be an insertion site in the vector as long as it contains a sequence which can be cleaved by a restriction endonuclease (see Eglitis et al. or Hillgenberg et al.). One of ordinary skill in the art would have been motivated to include insertion sites of the type recited in the claims in the vectors described by Perkins et al. because Eglitis et al. or Hillgenberg et al. teach that any insertion sites can be engineered into vectors in terms of multiple cloning sites or that any sequence of any size can comprise an insertion site as long as it comprises a restriction endonuclease cleavage site. The specific claimed sizes of insertion sites (i.e. 0, 1, 2, 4, 1,000, 5,000 bp) must be considered a matter of design choice since sequences of any size can comprise an insertion site for heterologous nucleic acids of interest. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perkins et al. in view of German et al. (US 6,225,290) or Huston et al. (US 6,207,804).

Applicant's invention is as described above. In addition, applicants claim that the proximal 5' regulatory sequences of the vector include a eukaryotic intron sequence or an intron sequence derived from intron 1 of a ferritin heavy chain gene.

Perkins et al. is applied as in the above rejection under 35 USC 102(e). Perkins et al. does not teach use of intron sequences in the 5' regulatory region of the vector.

German et al. (see whole document, particularly the paragraph bridging columns 7-8) and Huston et al. (see whole document, particularly column 15) teach the standard insertion of intron sequences in the 5' regulatory regions of expression vectors in order to enhance expression of genes operably linked to said regulatory regions. It is noted that the two cited references are two among hundreds of references reciting the desirability of including intron sequences in promoter regions of expression vectors so as to enhance expression.

The ordinary skilled artisan, seeking to design expression vectors as described by Perkins et al. would have been motivated to include intron sequences into the 5' regulatory region of the vector because inclusion of intron sequences in 5' regulatory regions of expression vectors had been a standard technique known in the art (see German et al. or Huston et al.) wherein the intron sequences served to enhance expression of the heterologous gene of interest. It would have been obvious for the ordinary skilled artisan to do this because inclusion of intron sequences into promoter regions in expression vectors so as to enhance expression was well known in the art

(see Huston et al. and German et al.). With regard to the inclusion of intron sequences **derived from** intron 1 of a heavy chain ferritin gene, the intron sequence is not limited to sequences naturally occurring in intron 1 because applicants define the term "derived from" as including sequences derived from a reference sequence by a combination of insertions, deletions and/or substitutions of one or more nucleotides in a reference sequence. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

35 USC 112, 1st Paragraph Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 64 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim vector pFerX11; however, the examiner can find so support in the application, as filed, for this newly claimed vector. This is a NEW MATTER rejection.

Claim 63 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D., can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

March 29, 2008

/David Guzo/
Primary Examiner
Art Unit 1636